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Functional Medicine

QUOTE GM #15 **17/11/2017**

Titre Créé le

NOUVELLES DÉCOUVERTES SUR LE POLYMORPHISME DU GÈNE DIO2 THYROÏDIEN

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DIO2 Thr92Ala Reduces Deiodinase-2 Activity and Serum-T3 Levels in Thyroid-Deficient Patients.

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Abstract

CONTEXT: A substantial proportion of athyreotic levothyroxine (LT4)-treated patients experience hypothyroid-like symptoms. During LT4 replacement, levels of the active hormone triiodothyronine (T3) strictly depend on type 2-deiodinase (D2)-mediated activation of LT4. The Thr92Ala polymorphism and the 258 G/A in the DIO2 gene have been associated with various clinical conditions.

OBJECTIVES: To investigate the effects of DIO2 polymorphisms in thyroid hormone homeostasis.

DESIGN: We compared the presurgical hormonal status of thyroidectomized LT4-treated patients who had a similar thyroid-stimulating hormone (TSH) level with their postsurgery status and analyzed their DIO2 genotype in a subgroup of 102/140 (72.8%) of patients. We measured the enzymatic properties of Thr92Ala in living cells and in relevant generated mouse models.

SUBJECTS AND METHODS: A total of 140 thyroidectomized subjects were included. Serum free T3 (FT3), free thyroxine, and TSH levels were directly measured. Immunohistochemistry and immunoblotting were performed for D2 protein.

RESULTS: The DIO2 genotyping revealed an association between low FT3 values and Thr92Ala. Specifically, the mean postsurgery FT3 levels were significantly lower in patients carrying the mutated allele(s) than in wild-type patients, in whom FT3 postsurgical levels were similar to presurgery levels. The -258 G/A variation was not associated with hormonal alteration. We found that endogenous wild-type D2 and Thr92Ala share the same subcellular localization but differ in protein stability. Importantly, Thr92Ala reduced D2-mediated thyroxine to T3 conversion.

CONCLUSIONS: Thyroidectomized patients carrying Thr92Ala are at increased risk of reduced intracellular and serum T3 concentrations that are not adequately compensated for by LT4, thus providing evidence in favor of customized treatment of hypothyroidism in athyreotic patients.

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"Contexte:
Une proportion importante des patients traités à la lévothyroxine athyrétique (LT4) présentent des symptômes de type hypothyroïdien. Pendant le remplacement du LT4, les niveaux de l'hormone active triiodothyronine (T3) dépendent strictement de l'activation du LT4 par la diiodinase de type 2 (D2). Le polymorphisme de Thr92Ala et le 258 G/A du gène DIO2 ont été associés à diverses conditions cliniques."

"Conclusions:
Les patients thyroïdectomisés porteurs de Thr92Ala sont plus à risque de réduire les concentrations intracellulaires et sériques de T3 qui ne sont pas adéquatement compensés par LT4, fournissant ainsi des preuves en faveur du traitement personnalisé de l'hypothyroïdie chez les patients athyréotiques."

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